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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/807,736	03/24/2004	Tetsuji Okuno	4-30961BC1C1	5416

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CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 104/3
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EXAMINER	
KWON, BRIAN YONG S	

ART UNIT	PAPER NUMBER
1614	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/807,736	OKUNO ET AL.	
	Examiner	Art Unit	
	Brian S. Kwon	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04/03/07*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-22* is/are rejected.

7)☐ Claim(s) _ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 March 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/989,577.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. Acknowledgement is made of applicant's filing of an amendment/remarks on 04/03/07. By the amendment claims 11-18 have been cancelled and claims 19-22 have been newly added.

2. Applicant's arguments have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set of actions being applied to the instant application.

3. Applicant's amendment changing the scope of the invention necessitates a new ground of the rejection in this Office Action.

Claim Objections

4. Claim 19 is objected to because of the following informalities: Improper Markush-type language is used. Applicant is suggested to amend "selected from...and" to "selected from the group consisting of...and...".

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 20 and 21-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Dependent claim 20 recites that the bisphosphonate is utilized "for the embolic treatment of angiogenesis". However, there is insufficient antecedent basis for this limitation in the claim 19 which is directed to a method of treating proliferative disease such as rheumatoid arthritis, osteoarthritis, breast cancer, colon cancer, small cell lung cancer, prostate cancer, diabetic retinopathy, psoriasis, haemangioblastoma and haemangioma. Apparently, this inconsistency leaves the reader in doubt as to the meaning of the invention to which they refer, thereby rendering the definition of the subject-matter of said claims unclear.

With respect to the applicant' recitation of term "the bisphosphonate acts to reduce angiogenesis" with " a method of treating a patient suffering from a proliferative disease", the examiner recognizes that he breadth of essential method step "the bisphosphonate acts to reduce angiogenesis" required in the instant invention is not consistent with the preamble of the claiming subject matter and renders the definition of the subject-matter of said claims unclear.

This rejection could be obviated by amending the claim to "an effective amount of a bisphosphonate wherein the bisphosphonate acts to reduce angiogenesis" to "an effective amount of a bisphosphonate to treat the proliferative disease by reducing angiogenesis".

Regarding claims 21-22, the claims recite the limitation "a pharmaceutically acceptable salt thereof or any hydrate thereof" in claim 19. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

6. Claims 19-21 are rejected under 35 U.S.C. 102(e) as being anticipated by Askew et al. (US 6048861).

Askew teaches the use of composition comprising integrin receptor antagonist, bisphosphonates (e.g., alendronate, pamidronate, risedronate, ibandronate, etidronate, etc...) and a vascular endothelial growth factor inhibitor for the treatment, prevention or inhibition of angiogenesis, macular degeneration, inflammation, diabetic retinopathy, atherosclerosis and tumor growth (abstract; column 34, lines 27-31 and claim 26).

Since the interpretation of the instant claims allow for the inclusion of any other unspecified ingredients even in major amounts in said composition, the reference anticipates the claimed invention.

Although Askew is silent about "embolic treatment of angiogenesis", such feature must be inherently presented in the referenced method of treating, prevention or inhibition of

angiogenesis, diabetic retinopathy and tumor growth The prior art directing the administration of bisphosphonates inherently possessing a therapeutic effect for the same ultimate purpose, for the treatment or prevention of angiogenesis, as disclosed by Applicants anticipates Applicants claim even absent explicit recitations of the mechanism of action.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Askew et al. (US 6048861) and further in view of Reszka et al. (US 6416964 B2).

The teaching of Askew has been discussed in above 35 USC 102(e) rejection. However, Askew is silent about the use of zoledronic acid or zoledronate for the claimed utility.

Reszka teaches zolendronate as functional equivalent of alendronate and pamidronate that is useful in the treatment or prevention of angiogenesis, macular degeneration, inflammation, diabetic retinopathy, atherosclerosis and tumor growth (column 1, lines 16-26; column 1, lines 56-59; column 1, line 65 thru column 2, line 3; column 2, lines 28-48; column 6, lines 32-42; column 7, line 49 thru column 10, line 29).

One having ordinary skill in the art would have been motivated to select the claimed compound with the expectation that substitution of zoldronate for alendronate or pamidronate would not significantly alter the analogous properties of the compound of the reference due to their known functional equivalency in the art. One would have been motivated to combine these references and make the modification because they are drawn to same technical fields (constituted with same ingredients and share common utilities), and pertinent to the problem which applicant concerns about. MPEP 2141.01(a).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. Claims 19-22 are rejected provisionally under the judicially created doctrine of double patenting over claims 9-10 of the copending application No. 10/484,482. This is a provisional obviousness-type double patenting rejection.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the scope of the instant invention overlaps the copending application.

Both of the instant application and the copending application are drawn to a method of treating proliferative diseases such as prostate carcinoma, lung cancer and melanoma comprising administering same bisphosphonate compounds, thus the copending application(s) make/makes obvious the instant invention.

Response to Arguments

9. Applicant's arguments filed 04/03/07have been fully considered but they are not persuasive.

Applicant's argument in the response takes the position that none of the references cited teach each and every element as set forth in the present set of claims found, either expressly or inherently.

This argument is not found persuasive. Unlike the applicant's argument, Askew et al. (US 6048861) teaches the use of composition comprising integrin receptor antagonist in combination

with the claimed bisphosphonates (i.e., alendronate, pamidronate, risedronate, ibandronate, etidronate, etc...) and a vascular endothelial growth factor inhibitor for the treatment, prevention or inhibition of angiogenesis, macular degeneration, inflammation, diabetic retinopathy, atherosclerosis and tumor growth (abstract; column 34, lines 27-31 and claim 26).

Since the interpretation of the instant claims allow for the inclusion of any other unspecified ingredients even in major amounts in said composition, the reference anticipates the claimed invention.

In response to applicant's argument that Askew fails to teach the activity of the instant bisphosphonate in reducing angiogenesis, such feature must be inherently presented in the referenced method of treating, prevention or inhibition of angiogenesis, diabetic retinopathy and tumor growth. The prior art directing the administration of same composition containing bisphosphonates inherently possessing a therapeutic effect for the same ultimate purpose as disclosed by Applicants anticipates Applicants claim even absent explicit recitations of the mechanism of action. Again, the fact that the applicant may have discovered a new pharmacological mechanism for bisphosphonate is not considered patentably distinctive over the prior art which are directed to the same therapeutic application (for the treatment of the treatment, prevention or inhibition of angiogenesis, macular degeneration, diabetic retinopathy, and tumor growth).

Anticipation under 35 USC 102 is an essentially irrebuttable question of fact, wherein the court stated that anticipation "cannot be overcome by evidence of unexpected results or teachings away in the art". *In re Malagari, 499 F.2d 1289, 182 USPQ; In re Spada, 911 F.2d 705, 15 USPQ2d 1655 (Fed. Cir. 1990); In re Fracalossi, 681 F.2d 792, 215 USPQ 569 (CCPA*

1982); In re Alternpohl, 500 F.2d 1151, 183 USPQ 38 (CCPA 1974); In re Wiggins, 488 F.2d 538, 179 USPQ 421 (CCPA 1973); In re Wilder, 429 F.2d 447, 166 USPQ 545 (CCPA 1970). Indeed, a reference might reside in a nonanalogous art and yet constitute an anticipation of a claimed invention under 35 USC 102. *In re Self, 571 F.2d 134, 213 USPQ 1 (CCPA 1982).*

Conclusion

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

11. No Claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (571) 272-0581. The examiner can normally be reached Tuesday through Friday from 9:00 am to 7:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached on (571) 272-0718. The fax number for this Group is (571) 273-8300.

Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications may be obtained from Private PAIR only. For more information about PAIR system, see http://pair-direct.uspto.gov Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).

Brian Kwon
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